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Increased Apoptosis in Patients with Major Depression: A Preliminary Study

Eran Eilat, ‡ Shlomo Mendlovic, 1* Adiel Doron, * Vera Zakuth, ‡ and Zvi Spirer ‡

Apoptosis is a programmed cell death that can be observed in normal cells. Major depression poses a combination of a depressed and destructive autoimmune reaction. We measured apoptosis in the PBLs of seven patients with major depression and in age- and sex-matched controls. We observed significantly increased apoptosis in the PBLs of depressive patients (p < 0.05). These preliminary results could contribute to an understanding of the interactions of the CNS with the immune system, which could lead to the increased vulnerability of the CNS in depressive disorders. Further studies are needed to establish these results. The Journal of Immunology, 1999, 163: 533–534.

A poptosis is a normal physiological programmed cell death that can be enhanced by a variety of external stimuli, such as viral infections, medications (i.e., anticancer treatments), and pathological conditions (e.g., autoimmune diseases and degenerative diseases of the CNS) (1). This phenomenon can be mediated via various pathways that cause condensation of the cytoplasm and chromatin, nuclear fragmentation, and ultimate sequestration of cellular contents into membrane-bound apoptotic bodies (2). Major depression is a common disorder, with a lifetime prevalence of ~15%. Moreover, it may be a life threatening condition, as 30% of all depressive patients attempt suicide and 10% eventually commit suicide (3). Major depression has been shown to be associated with various immune abnormalities, although the findings have not been consistently demonstrated (4).

We hypothesized previously that depressive patients can exploit their immune system for suicide (5), and one of the possible mechanisms includes apoptosis. Therefore, we measured the apoptotic cells in PBLs of depressive patients and normal age- and sex-matched controls.

Materials and Methods

Patients

Of >500 patients referred to the psychiatric facilities affiliated with the Shalvata Mental Health Center, nine patients (six males and three females; age 51.7 ± 12) and nine age- and sex-matched controls (age 50.8 ± 15) entered the study. Two couples were excluded due to prolonged delay in blood delivery. The inclusion criterion was major depression (diagnosed according to DSM-IV (Diagnostic and Statistical Manual) criteria) that lasted 2–12 wk. The exclusion criteria were age younger than 18 years; any other major psychiatric disorder (e.g., schizophrenia, substance abuse, and reactive depression); medication by antidepressive, antipsychotic, or anxiolytic drugs; usage of immune-affecting medications; any immunological or hematological disorder; and an infectious disease (localized or generalized) in the month before examination. These stringent exclusion criteria were applied because antidepressive and anxiolytic medications are known to alter various immune functions (6, 7). The controls were randomly selected from a pool of healthy persons who agreed to participate in the study. Matching was done by sex and age criteria.

After a full explanation and informed consent, depression, anxiety, and suicidal tendency were assessed by the Hamilton Depression Rating Scale, Hamilton Anxiety Rating Scale, and Beck Depression Inventory questionnaires, respectively.

Peripheral blood (25 ml) was drawn via venous puncture. Blood was transported and analyzed within 2 h. Apoptosis was assessed by flow cytometry using Apoptest Ylem, Avezzano, Italy), which is based on the increased stainability of lymphoid cells on the part of newly developed fluorophores that occur during the early phases of apoptosis, as described previously (8). In brief, whole blood was lysed within <2 h; cells were stained for Apo stain, fixed (with 4% paraformaldehyde), and evaluated in a FACScan flow cytometer (Becton Dickinson, Mountain View, CA) with excitation at 650 nm (FL3 channel). Cells were gated on lymphocytes and evaluated as a percentage of whole cells.

Statistical analysis

For statistical evaluation of the apoptotic cells in depressive patients and healthy controls, we used Wilcoxon’s signed-rank test.

Results

Table I demonstrates depression and anxiety scores and the apoptotic cells as a percentage of whole PBLs in depressive patients and their matched controls. The depressed patients had a significantly higher Hamilton depression rating score (25.85 ± 6.4) compared with the controls (0.4 ± 0.7). Similar findings were seen for the Hamilton anxiety rating scale (29.85 ± 7.1 in depressive patients vs 1 ± 1.9 in controls). In Fig. 1, we demonstrate the percentage of apoptotic cells in depressive patients and their matched controls; a significant increase in apoptosis was observed in the depressive patients (p < 0.05).

Discussion

In patients with major depression, various immunological abnormalities were observed, such as reduced NK cell activity (9, 10, 11) and decreased T cell function (12). In the present study, we observed an increased tendency for apoptosis of PBLs. We observed a wide range of apoptosis in the normal controls and in the
and controls.

Figure 1. Percentage of apoptotic cells in PBLs of depressive patients and controls.

Table 1. Depressive and anxiety scores and percentage of apoptosis in PBLs in depressive patients and controls

<table>
<thead>
<tr>
<th>Patient</th>
<th>Depressed Patient Score (%)</th>
<th>Control Patient Score (%)</th>
<th>Depressed Patient Apoptotic Cells (%)</th>
<th>Control Patient Apoptotic Cells (%)</th>
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<td>Anxiety Score (patients)</td>
<td>Cells (%)</td>
<td>Score (control)</td>
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* F, female; M, male.

References